

## Original

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# Initial clinical outcomes and prognostic variables in the implementation of a Code Sepsis in a high complexity University Hospital

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## ABSTRACT

**Objectives.** To assess the impact of the first months of application of a Code Sepsis in a high complexity hospital, analyzing patient's epidemiological and clinical characteristics and prognostic factors.

**Materials and methods.** A long-term observational study was carried out throughout a consecutive period of seven months (February 2015 – September 2015). The relationship with mortality of risk factors, and analytic values was analyzed using uni- and multivariate analyses.

**Results.** A total of 237 patients were included. The in-hospital mortality was 24% at 30 days and 27% at 60 days. The mortality of patients admitted to Critical Care Units was 30%. Significant differences were found between the patients who died and those who survived in mean levels of creatinine (2.30 vs 1.46 mg/dL,  $p < 0.05$ ), lactic acid (6.10 vs 2.62 mmol/L,  $p < 0.05$ ) and procalcitonin (23.27 vs 12.73 mg/dL,  $p < 0.05$ ). A statistically significant linear trend was found between SOFA scale rating and mortality ( $p < 0.05$ ). In the multivariate analysis additional independent risk factors associated with death were identified: age  $> 65$  years (OR 5.33,  $p < 0.05$ ), lactic acid  $> 3$  mmol/L (OR 5.85,  $p < 0.05$ ), creatinine  $> 1.2$  mgr /dL (OR 4.54,  $p < 0.05$ ) and shock (OR 6.57,  $P < 0.05$ ).

**Conclusions.** The epidemiological, clinical and mortality characteristics of the patients in our series are similar to the best published in the literature. The study has identified several markers that could be useful at a local level to estimate risk of death in septic patients. Studies like this one are necessary to make improvements in the Code Sepsis programs.

**Key-words:** Sepsis, code sepsis, mortality

## Resultados clínicos iniciales y variables pronósticas en la implementación de un Código Sepsis en un Hospital Universitario de alta complejidad

## RESUMEN

**Objetivo.** Evaluar el impacto de un programa educativo y organizativo llamado Código Sepsis, en los primeros siete meses de su aplicación en un hospital de alta complejidad.

**Material y métodos.** Se realizó un estudio observacional durante un período consecutivo de siete meses (Febrero 2015-Septiembre 2015). Se analizó la relación con la mortalidad de los factores de riesgo y los valores analíticos usando análisis uni y multivariante.

**Resultados.** Se incluyeron un total de 237 pacientes. La mortalidad intrahospitalaria a los 30 días fue del 24 % y del 27% a los 60 días. La mortalidad de los pacientes ingresados en Unidades de Cuidados Críticos fue del 30%. Se encontraron

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diferencias significativas entre los pacientes que murieron y los que sobrevivieron en sus valores medios de creatinina (2,30 vs 1,46 mg/dL,  $p < 0,05$ ), ácido láctico (6,10 vs 2,62 mmol/L,  $p < 0,05$ ) y procalcitonina (23,27 vs 12,73 mg/dL,  $p < 0,05$ ). Se encontró una tendencia lineal estadísticamente significativa entre los valores de la escala SOFA y la mortalidad ( $p < 0,05$ ). En el análisis multivariante se identificaron otros factores de riesgo independientes asociados con la muerte: edad  $> 65$  años (OR 5,33,  $p < 0,05$ ), ácido láctico  $> 3$  mmol/L (OR 5,85,  $p < 0,05$ ), creatinina  $> 1,2$  mgr/dL (OR 4,54,  $p < 0,05$ ) y el shock (OR 6,57,  $P < 0,05$ ).

**Conclusiones.** La mortalidad en este estudio se encuentra dentro de los límites de los ensayos clínicos más recientes de sepsis. El estudio ha identificado varios marcadores que podrían ser útiles a nivel local para estimar el riesgo en pacientes sépticos. Estudios como éste son necesarios para hacer mejoras en los programas de Código Sepsis

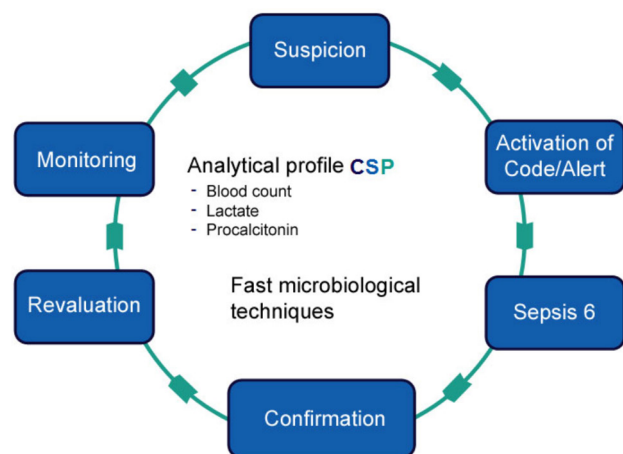
**Palabras clave:** Sepsis, código sepsis, mortalidad.

## INTRODUCTION

Currently sepsis is a pathology which still shows a high mortality rate; the present consensus is that early and effective treatment of these patients is key to improving their healthcare outcomes.

One of the initiatives which have contributed to improve care of these patients in Spain is the implementation of Code Sepsis programs in hospitals under the auspices of a National Code Sepsis Network [1].

These activation codes are the result of applying strategies for the coordination of different assistance levels involved in time-dependent pathologies. These codes are implemented, with the aim of early detecting patients suffering from life-threatening events (stroke, heart attack...) and triggering the activation of measures necessary to improve their prognosis [2].



**Figure 1** Flowchart for care of patients with Code Sepsis Alert activation

The Code Sepsis of University Hospital of La Princesa (CSP) [3] is a set of clinical, organizational, analytical and microbiological tools that, used together with intensive training and cognitive support, has the mission of improving the care of septic patients. It prioritizes care and fine-tuning treatment and enables simple and efficient clinical work.

The objective of this study was to assess the first months of application of a Code Sepsis in a high complexity hospital, describing the outcomes and defining the prognosis variables.

## MATERIAL AND METHODS

**Intervention: Code Sepsis Princesa 2015.** The Code Sepsis was launched in February 2015 after 12 meetings held throughout 2014 of a multidisciplinary group originally composed of professionals from the departments of Internal Medicine, Intensive Care Medicine, Anesthesia and Surgical Critical Care, Emergency Medicine, Microbiology, Clinical Analysis, Admission and Clinical Documentation and General Surgery, and later by Nursing, Preventive Medicine, Radiology, and Urology, among others. Also, during 2014, prior to Code launch, 14 sessions explaining the Code Sepsis were held in different hospital departments, and 4 courses of 20 hours were conducted to train experts in sepsis for a total of 80 doctors and nurses. The Code was disseminated throughout the hospital by means of teaching materials in the form of cognitive aids and a hospital general session.

The CSP is based on the application of a sequence of coherent clinical decisions (figure 1).

When sepsis with organ failure was suspected, a Code Sepsis alert was activated in the Electronic Health Record of the hospital and *sepsis six (bundle in the first hours)* was initiated with the administration of oxygen, antibiotics and fluids, and obtaining an analytical profile and cultures. Later when the alert was confirmed, and the patient was reevaluated in less than three hours to decide whether to continue the treatment at the diagnosis site (emergency department, wards ...) or to relocate the patient to a Critical Care Unit due to poor evolution.

To facilitate the diagnosis and stratification of patients with CSP Alert, the clinicians had available a specific analytical tool for sepsis that includes a scalable request, including determinations of complete blood count, including platelets, arterial or venous blood gas, including oxygen and CO<sub>2</sub>, blood pressure and lactic acid, biochemical analysis with creatinine, bilirubin and procalcitonin, some of them necessary for the calculation the Sequential Organ Failure Assessment score (SOFA).

Blood cultures and other cultures from the suspected focus of infection are recommended.

They are prioritized in those patients with CSP alert, using rapid detection techniques available in the hospital like MALDI-TOF or GenomERA, and detection of *S. pneumoniae* antigen by a rapid immunochromatographic assay (ICT).

In order to disseminate knowledge of the CSP, training is

carried out through specific courses for the hospital physicians and nurses experts in sepsis and through general training sessions in the services most often involved.

The following consensus documents, among others, were elaborated and placed in the document directory of the hospital information system:

- CSP protocol: a set of recommendations on suspicion, rapid diagnosis, hemodynamic resuscitation and early administration of antibiotics, and a guide for the tools and protocol summary.
- Antibiotic treatment guide, with high doses adapted to septic patient.
- Sample and culture collection protocols.

**Design and variables of the study.** An analytical observational prospective study was carried out on all patients with an activation of the CSP alert, from February 1, 2015 to September 30, 2015. Only patients with "severe sepsis" (with sepsis and organ failure in Sepsis-2 definitions) were included in the CSP alert in 2015. "Sepsis" according to the new 2016 definitions (Sepsis-3) is like severe sepsis [4]. There were no exclusion criteria. The study included patients with alerts activated anywhere in the hospital: Emergency Department, hospital wards, Critical Care Units.

Socio-demographic factors (age, sex), infection risk factors (acute renal failure, diabetes mellitus, immunosuppression, antibiotic treatment in the three previous months), and other severe risk factors such as admission to critical care units and the Sequential Organ Failure Assessment (SOFA) score were collected.

Analytical data collection was carried out in three stages: in the first 6 hours after the alert activation, from 6 to 12 hours and at 12 hours after activation. In each of these stages hematocrit, leukocytes, platelets, bilirubin, creatinine, lactic acid and procalcitonin were determined. Also a number of microbiological culture tests were carried out to identify microorganisms.

The fluid management was registered in the first 6h and 12h. All the antibiotics administered to the patient and the need for fluid resuscitation in the first 24 hours were also registered.

Outcome variables were overall mortality at 30 and 60 days and in hospital length of stay.

A prognostic risk variable was created, which combined lactic acid  $\geq 3$  mmol/L and procalcitonin  $\geq 2$  mg/dL in the first 6 hours. According to this variable, patients were classified as: "low risk", if both indicators were below their threshold; "moderate risk", if only one of them was above threshold and "high risk" if both were above threshold.

Also another composite variable was created combining Shock Index (heart rate/systolic blood pressure)  $\geq 0.8$  and lactic acid  $\geq 3$  mmol/L.

An antibiotic was considered "adequate antibiotic" if it was administered according to the hospital guidelines for

the suspected focus of infection and / or the microorganisms isolated in the previous cultures were sensitive and the doses applied followed the recommendations of the hospital commission for infections for Code Sepsis.

Finally, the number of antibiotics administered in the first 3 hours, between 3 and 6 hours and after 6 hours from the activation of the Code Sepsis were also registered

**Statistical analysis.** For qualitative variables their frequency and percentage were determined. The  $\chi^2$  test or the Fisher nonparametric test was used for their comparison.

For quantitative variables the mean and standard deviation (SD) were calculated. Comparisons were carried out with the Student t Test or the nonparametric Mann-Whitney U test.

An explanatory model of mortality with logistic regression was constructed, which included all the variables that were statistically significant in the univariate analysis, calculating the corresponding odds ratio (OR) for each of the variables.

Statistical significance was established as  $p < 0.05$ . The analyses were carried out with Statistics Software SPSS Version 19 and Stata / SE, version 13 (Stata Corp, College Station, TX).

The study was approved by the Ethics committee for Clinical Research of La Princesa University Hospital, Registration number PI-893.

## RESULTS

A total of 237 patients were included. Seventy nine percent (188) of the CSP alerts were activated in the Emergency Department and 33% (79) of the total cases needed to be admitted to the Critical Care Units. The distribution of the clinical and epidemiological characteristics, risk factors and severity are presented in table 1.

The mean inpatient length of stay was 15 days (SD 28) and the mean length of stay in the Critical Care Units was 9 days (SD 16). The source of the infection was abdominal in 31.4% (75) of the cases, respiratory in 30.5% (73) and urological in 26.4% (63).

Of the 470 cultures taken, 204 were blood cultures (36% positives), 133 urine cultures (37% positives), 46 respiratory samples (24% positives), 32 stool cultures (37.5% positives), 22 abdominal fluid samples (68% positives), 15 skin and soft parts (66% positives), 8 central line catheters (25% positives) and 10 other samples (30% positives). Table 2 shows the more frequent isolated microorganisms depending on antibiotic onset. Eleven percent (36) of the isolated microorganisms were multi-resistant; the most frequent were: carbapenem resistant (OXA-48 was the most frequent carbapenemase) and extended-spectrum  $\beta$ -lactamase producing *Klebsiella pneumoniae* (19%), extended-spectrum  $\beta$ -lactamase producing *Escherichia coli* (16%), and *Pseudomonas aeruginosa* multidrug-resistant (11%).

Changes in biomarker concentrations in the first 24 hours of CSP activation were statistically significant. In the case of lactic acid, its mean values were 3.47 mmol/L (SD 3.17) in the

first six hours (0–6 h), 2.99 mmol/L (SD 3.86) (6–12h), 2.02 mmol/L (SD 1.68) (12–24h) ( $p < 0.05$ ). Regarding procalcitonin, its mean values were the following: 15.04 mg/dL (SD 26.32) (0–6h), 23.85 mg/dL (SD 29.97) (6–12h) and 22.53 mg/dL (SD 33.65) (12–24 h) ( $p < 0.05$ ).

Significant differences were found between the patients who died and those who survived in mean levels of creatinine (2.30 vs 1.46 mg/dL,  $p < 0.05$ ), lactic acid (6.10 vs 2.62 mmol/L,  $p < 0.05$ ) and procalcitonin (23.27 vs 12.73 mg/dL,  $p < 0.05$ ).

With respect to the recommended measures in the approach to sepsis, 38% (90) of the patients received more than 2L of crystalloids in the first 6h and 29% (79) more than 4L in the first 24h. Thirty five percent of the patients needed vasopressors after resuscitation with fluids. Three hundred-ninety antibiotics were administered in total; 56% in the first 3h after the activation, 15% between 3 and 6h, and 29% after 6 hours.

The 81% of the antibiotics administered were considered adequate.

At 30 days the overall hospital mortality was 24% (56). At 60 days, mortality was 27% (63); 63% (150) of the patients were at home and 10% (24) remained hospitalized or in a medical care home. The mortality of the patients admitted to the Critical Care Units was 30% (24) and the mortality in hospital wards was 20.3% (32).

At the time of CSP alert, in those patients admitted to the Critical Care Units, the SOFA score was between 0 and 6 in 29 cases (45%), between 7 and 9 in 19 cases (29%) and above 10 in 17 cases (26%). We found a statistically significant linear tendency between the SOFA rating and mortality at both 30 days ( $p < 0.05$ ), and 60 days ( $p < 0.05$ ).

Figure 2 shows the percentages of mortality according to the SOFA group in those cases where the alert was activated in Emergency Department, in those where it was activated in the rest of the departments and in the patients who were admitted to the Critical Care Units.

Analyzing the possible relationship of patient comorbidity variables and clinical-analytical data with mortality, the risk factors identified were: age, creatinine, lactic acid, bilirubin, and procalcitonin in the first 6h (table 3).

A relationship was found between the patients with a Shock Index  $\geq 0.8$  and lactic acid  $\geq 3$  mmol/L in the first 6h of the activation and mortality ( $p < 0.05$ ). Death was 2.5 times more likely in these patients.

Analysis of the new prognostic risk variable (lactic acid  $\geq 3$  mmol/L and procalcitonin  $\geq 2$  mg/dL) showed that 30% of the cases were "low risk", 42% "moderate risk" and 28% "high risk", with a statistically significant relationship between risk and mortality ( $p < 0.05$ ). The risk of dying was 1.5 times higher in moderate risk patients and 8 times higher in high risk patients compared to low risk patients.

A statistically significant relationship was found between the administration of a single antibiotic or more than 2 antibiotics and mortality, even stratifying by the SOFA score ( $p < 0.05$ ). However, this did not occur with the administration

**Table 1** Characteristics of patients included in Code Sepsis

General data	
Age, years (SD)	72 (15)
Sex: Men, n (%)	141 (60)
Hospitalization in the previous 3 months, n (%)	80 (34)
Antibiotics in the previous 3 months, n (%)	73 (31)
Service: emergencies, n (%)	188 (79)
Comorbidity	
Renal insufficiency, n (%)	45 (19)
Diabetes mellitus, n (%)	65 (27)
Immunosuppression, n (%)	51 (21)
Hypertension, n (%)	125 (53)
Ischemic cardiopathology, n (%)	35 (15)
Stroke, n (%)	20 (8)
Neoplasia, n (%)	62 (26)
Clinical data and analyses	
HR, bpm (SD)	104 (25)
SBP, mmHg (SD)	107 (28)
Hematocrit, % (SD)	38 (7.5)
Leukocyte /L (SD)	11,916 (12,526)
Platelets /L (SD)	180,672 (156,527)
Lactic acid, mmol/L (SD)	3.5 (3.2)
Procalcitonin, mg/dL (SD)	15 (26)
Creatinine, mg/dL (SD)	1.6 (1.1)
Bilirubin, mg/dL (SD)	1.3 (1.4)
PaO <sub>2</sub> /FiO <sub>2</sub> (SD)	262 (123)
SAO <sub>2</sub> /FiO <sub>2</sub> (SD)	164 (157)
Severity data	
SOFA (SD)	7.8 (4.6)
APACHE (SD)	19.3 (7.9)
Admission Crit. Care U., n (%)	79 (33)
Stay in Crit Care U. in days (SD)	9 (16)
Global stay in days (SD)	15 (28)
Mortality at 30 days, n (%)	56 (24)
Mortality at 60 days, n (%)	63 (27)

SD: Standard deviation; n: frequency; HR: Heart rate; bpm: beats per minute; SBP: Systolic blood pressure; SOFA: Sepsis related Organ Failure Assessment; APACHE: Acute Physiology and Chronic Health Evaluation; Crit.Care U.: Critical Care Units

of two antibiotics, where the percentage of mortality was 0%. The association of total number of antibiotics with mortality after 6h showed a linear tendency ( $p < 0.05$ ).

In the multivariate analysis of mortality, some associated fac-

**Table 2** Isolated microorganisms according to antibiotic onset.

Before Antibiotic Onset (N=119)	n (%)
<i>Escherichia coli</i>	33 (28)
<i>Klebsiella pneumoniae</i>	13 (11)
<i>Enterococcus faecalis</i>	10 (8)
<i>Staphylococcus epidermidis</i>	8 (7)
<i>Pseudomonas aeruginosa</i>	7 (6)
<i>Streptococcus pneumoniae</i>	7 (6)
<i>Staphylococcus hominis</i>	6 (5)
Rest	35 (29)
During Antibiotic Treatment (N=187)	n (%)
<i>Escherichia coli</i>	45 (24)
<i>Enterococcus faecalis</i>	12 (6)
<i>Enterococcus faecium</i>	11 (6)
<i>Klebsiella pneumoniae</i>	10 (5)
<i>Staphylococcus epidermidis</i>	9 (5)
<i>Candida albicans</i>	8 (4)
Methicillin-resistant <i>S. aureus</i>	7 (4)
<i>Staphylococcus aureus</i>	6 (3)
Rest	76 (42)

N: total number; n: frequency

tors were identified independently: age, lactic acid, creatinine and shock (need for vasopressors) (table 4). With the combination of these factors, a new variable was created that classified patients according to the presence or absence of 1, 2, 3 or 4 of the identified factors. Thus, 17 patients (7%) were  $\geq 65$  years of age, showed lactic acid  $\geq 3$  mmol/L, creatinine  $\geq 1.2$  mg/dL and need for vasopressors (Shock), 13 of which (76.5%) died. A statistically significant relationship was found between this new variable and mortality, with a significant linear trend, where the number of associated risks correlated positively with the risk of mortality ( $p < 0.05$ ).

## DISCUSSION

The benefit of activating "Code Sepsis" in a septic patient is the speed of reaction in a time-dependent pathology: quick diagnosis due to prioritization in the involved departments (Microbiology, Clinical Analysis, Radiology) and speed in the treatment, prioritizing the need of surgical or interventional drainage of the focus as well as the early evaluation by Critical Care Units if necessary.

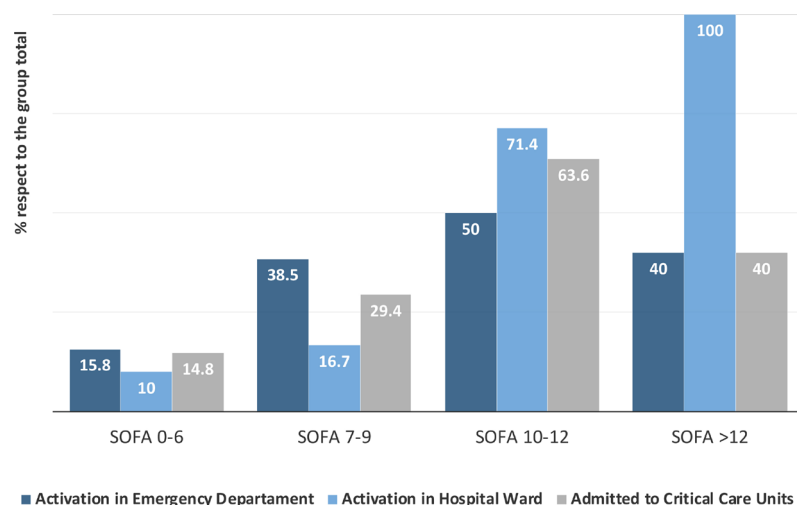
The results of the patients analyzed highlight as opportunities for improvement the need to perform an early identification, the need for faster resuscitation and the administration of the antibiotic within the first hour of Code activation.

The results of the first few months of application of the CSP model are mainly in agreement with the data published in the most important recent national [5-7] and international studies on sepsis [8-10].

The mean age of the patients in this study is higher than that of the patients in the above mentioned publications, while their characteristics do not show any other relevant difference. The suspected or confirmed sources of infection are also in line with those already published. These data make the morbidity and mortality outcomes comparable with those of trials and publications.

The death rates in the above mentioned publications are between 19 and 28%, comparable to 24% found in our study. It is interesting to highlight the high percentage of survivors (63%), who are at home at 60 days.

Length of stays in Hospital and Critical Care Units are longer in this study than in the international ones, although they are similar to the few national studies published, which may not only reflect the higher severity of the cases, but also differences in clinical practice in different countries. In fact, one of the most notable circumstances is the low number of admissions to the Critical Care Units in our sample, 33% compared with an average of nearly 80% in international studies for the same profile of patients [5-7].



**Figure 2** Percentage of mortality in different SOFA scale groups according to the location of Code Sepsis Alert Activation and admitted in Critical Care Units.



**Table 3** Univariate analysis of association between risk or predictive factors and death.

	Deaths		OR (CI 95%)	p
	YES	NO		
Age > 65 years old, n (%)	50 (29)	6 (9)	4.56 (1.85 – 11.21)	0.001
Sex: Men, n (%)	34 (24)	22 (23)	1.07 (0.60 – 1.97)	0.831
Renal insufficiency, n (%)	13 (29)	43 (22)	1.40 (0.68 – 2.91)	0.358
Diabetes mellitus, n (%)	16 (25)	40 (23)	1.07 (0.55 – 2.09)	0.826
Immunosuppression, n (%)	12 (24)	44 (24)	0.99 (0.47 – 2.06)	0.985
Hypertension, n (%)	30 (24)	26 (23)	1.04 (0.57 – 1.90)	0.887
Ischemic Cardiopathology, n (%)	8 (23)	48 (24)	0.95 (0.40 – 2.23)	0.907
Stroke, n (%)	3 (15)	53 (24)	0.54 (0.15 – 1.93)	0.349
Neoplasia, n (%)	19 (31)	37 (21)	1.65 (0.85 – 3.15)	0.132
Hospitalization in the previous 3 months, n (%)	19 (24)	37 (24)	1.01 (0.53 – 1.90)	0.975
Antibiotic in the previous 3 months, n (%)	13 (18)	43 (26)	0.61 (0.390 – 1.22)	0.162
Need for health care, n (%)	11 (31)	45 (22)	1.60 (0.72 – 3.51)	0.242
Heart rate, bpm (SD)	103 (29)	104 (23)	0.99 (0.98 – 1.01)	0.925
Systolic blood pressure, mmHg (SD)	107 (29)	108 (28)	0.99 (0.99 – 1.00)	0.811
Hematocrit, % (SD)	36 (8.7)	38 (7.1)	0.96 (0.92 – 1.00)	0.066
Leucocytes, thousand/mm3 (SD)	12.31 (10.4)	11.80 (13.1)	1.00 (0.99 – 1.00)	0.793
Platelets, thousand/mm3 (SD)	210.36 (216)	171.81 (133)	1.00 (0.99 – 1.00)	0.117
Bilirubin, mg/dL (SD)	1.81 (2)	1.09 (1)	1.36 (1.04 – 1.78)	0.024
Lactic acid > 3 mmol/L, n (%)	39 (42%)	15 (12%)	1.56 (1.27 – 1.83)	0.000
Procalcitonin > 2 mg/dL, n (%)	22 (29%)	8 (13%)	1.21 (1.02 – 1.44)	0.025
Creatinine >1.2 mg/dL, n (%)	33 (33%)	23 (17%)	1.23 (1.06 – 1.44)	0.004

n: frequency; SD: Standard Deviation; bpm: beats per minute; OR: Odds Ratio; CI: Confidence Interval

The combined use of two antibiotics shows significantly better results in these patients compared to using only one or a higher number of antibiotics, reflecting the possibility of adjusting clinical practice to the new Surviving Sepsis guidelines with respect to antibiotic treatment in combination with sepsis [11, 12].

Almost 20% of the antibiotics administered were not adequate, detecting an improvement opportunity, for example implementing microbiological techniques that accelerate the results of sensitivity to the microorganisms that cause sepsis.

With respect to resuscitation with crystalloids, the values are lower than those recorded in published studies, with a percentage lower than 40% for patients who were administered 2 litres in the first 6 hours and 4 litres in the first 24 hours. These results point to another possibility of improvement [13].

The mean initial values of the biological markers (lactic acid, procalcitonin and creatinine) are significantly higher in the patients who die with respect to those who survive, reflecting its usefulness as objective markers of severity in these patients [14–16].

The SOFA score, important in the light of the new definitions (Sepsis-3), allows us to easily stratify risk and shows a linear correlation with mortality, especially in patients hospitalized in medical ward. These patients show the highest SOFA values, indicating a delay in the activation of the CSP, which is related to higher death rates [17, 18].

In this study, some local risk scales were created by associating rates and markers, assessing their usefulness to identify severity and thus to be used in the location, re-evaluation and allocation of resources to these patients, as recommended by current precision medicine [19]. In the case of initial lactic acid higher than 3mmol/L and procalcitonin higher than 2mg/dL, we find an association with mortality in keeping with the literature, especially when both are high [20]. This is an interesting scale as it is an objective biological marker which evaluates infection and perfusion.

The combination of clinical variables and biological markers also seems very interesting in order to adjust the risk of patients in our hospital due to its simplicity of application

According to this study, when the combination of high Shock Index and high levels of lactic acid is applied, there is

**Table 4** Multivariate analysis of factors associated with death.

	n (%)	OR (CI 95%)	p
Age > 65 years	171 (72)	5.33 (1.08 – 26.38)	0.040
Lactic acid > 3 mmol/L	93 (42)	5.85 (1.67 – 20.46)	0.006
Creatinine >1.2 mg/dL	101 (43)	4.54 (1.01 – 20.43)	0.049
Need for Vasopressors (Shock)	71 (35)	6.57 (1.62 – 26.57)	0.008
Procalcitonin > 2 mg/dL	77 (56)	0.86 (0.21 – 3.49)	0.834
Shock index >0.8	166 (70)	0.23 (0.05 – 1.06)	0.059
Adequate Antibiotic therapy	191 (81)	4.51 (0.86 – 23.67)	0.075

n: frequency; OR: Odds Ratio; CI: Confidence Interval

a clear association with mortality. Therefore, this scale may be used in our local practice [21, 22].

In the multivariate analysis we have found that age, lactic acid, creatinine and shock as factors related to mortality, thus emphasizing the importance of adequate resuscitation in the outcome of sepsis patients.

The results suggest a very similar situation to the best results of our environment. The opportunities for improvement are clear in resuscitation and antibiotic treatment. Our results suggest avoiding excessive administration of antibiotics in the first few hours, as is defined in the recommendation for a rational start of antibiotic treatment [23].

The use of biomarkers and composite local ranges is a practice increasingly recommended in the context of precision medicine [19] and it is an opportunity for innovation, which may help improve patient prognosis and reduce the overuse of resources [24, 25].

The fundamental limitation of this study is that it does not compare septic patients before and after the implementation of CSP. At this moment, with the results of this study, we have an analysis of the situation at the beginning of the project, which gives us an opportunity to analyze its efficiency when compared to future stages

Moreover, as a result of new sepsis definitions and the campaign "Survive Sepsis 2016", an updating of CSP was carried out [11]. In this update, measures were included for the earlier activation of the alerts and for faster diagnostic tests along with the use of local risk scales which combine clinical indexes such as the new National Early Warning Score (NEWS 2) [26] with biomarkers. An evaluation of the 2016 and 2017 results is currently underway, in order to compare them with previous CSP results and implement the necessary measures to continue improving.

Sepsis is still an illness which causes death in one in four

patients affected by sepsis, and thus must continue being a priority in the hospital care; Code Sepsis is an opportunity for improvement in patient care.

## FUNDING

None to declare.

## CONFLICT

The authors declare that they have no conflicts of interest.

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